CASE REPORT

Monoclonal antibody Rituximab for severe immune thrombocytopenia after pegylated interferon for hepatitis C infection

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Abstract

Background: Severe immune thrombocytopenia displays a rare side effect of pegylated interferon therapy for Hepatitis C infection. Our aim is to report a case of severe and late onset immune thrombocytopenia due to pegylated interferon treatment that was effectively managed with the anti-CD20 monoclonal antibody Rituximab.

Description of the case: A 27-year-old male, Hepatitis C infected patient, presented with sudden, severe immune thrombocytopenia at the end of a standard 24-week antiviral treatment, as a side effect of pegylated interferon. Platelet count rapidly normalized with Rituximab infusions.

Conclusion: Rituximab could be a valuable treatment option in pegylated interferon related immune thrombocytopenia, when patients are resistant to conventional treatment or when physicians are reluctant to administer corticosteroids.

Keywords: Immune thrombocytopenia, pegylated interferon, HCV, Rituximab

Introduction

Thrombocytopenia is a common haematological abnormality diagnosed in patients affected with hepatitis C virus (HCV), and as well as an expected side effect of pegylated interferon (PEG-INF) treatment. Nevertheless, severe immune thrombocytopenia (platelets <25,000/µL) is a rare side effect of PEG-INF. The pathogenic mechanism possibly involves an interaction between platelets, antigen-presenting cells, T and B cells, evolving after the drug-dependent antibodies are directed against prevalent glycoproteins of the platelets’ surface. This event signals the CD4+ T helper cells activation, and eventually the B-cell differentiation and autoantibody production that opsonize platelets, promoting phagocytosis. Treatment of immune thrombocytopenia associated with PEG-INF therapy can be achieved with the monoclonal antibody Rituximab, that raises platelet counts in patients with immune thrombocytopenia by depleting the CD20-positive auto-reactive antibody-producing B cells.

Description of case

The patient reported is a 27-year-old male, who was diagnosed with HCV infection, after he was found on routine laboratory evaluation to have elevated aminotransferases. Anti-HCV antibodies in serum were positive and reverse transcriptase polymerase chain reaction (PCR) detected the HCV-RNA. The analysis of HCV-RNA revealed that the patient was infected with genotype 3a. Baseline platelet counts were within the lower normal limits; neutrophil counts, hematocrit, coagulation and other biochemical markers were normal. Liver biopsy showed mild histologic changes of chronic viral hepatitis and absence of significant fibrosis. The patient was treated with PEG-INF (180 µg sc weekly) and ribavirin (800 mg daily) for a total of 24 weeks. After treatment completion, circulating HCV RNA was undetectable.

During the 24 weeks of therapy the patient developed thrombocytopenia with platelets around 80,000/µL that remained at this level, without any other side effects or autoimmune disorders. At the time the treatment was discontinued, severe thrombocytopenia, as low as 4,000/µL presented, without hemorrhagic manifestations (Figure 1). Secondary causes of thrombocytopenia (lymphoproliferative, autoimmune, thyroid disorders) were excluded by laboratory evaluation and bone marrow examination that was suggestive of peripheral platelets destruction. An impending immunologic mechanism, as a late onset complication of PEG-INF, was assumed to be responsible. We infused, as first line treatment, high dose immunoglobulins (400 mg/kg) for five consecutive days, with no efficacy. We did not attempt to use corticosteroids. Then, the anti-CD20 monoclonal antibody Rituximab (375 mg/m² weekly for 4 weeks), was administered. After Rituximab infusion, the platelet count gradually normalized (Figure 1). The patient responded completely, did not present any other complications as result of treat-
tially followed by Rituximab weekly infusions. This report is of interest in certain aspects. It describes a case of immune thrombocytopenia due to PEG-INF treatment for Hepatitis C, with extremely low platelet counts, that occurred during treatment completion. In a large cohort of 979 HCV-infected patients treated with PEG-INF, severe thrombocytopenia defined as a platelet count of less than 50,000/μL was reported overall in 6.1% and only two patients had nadir platelet counts of <10,000/μL. In this study the incidence of severe thrombocytopenia after the 24 week of PEG-INF treatment ranged from 0.3-2.5% depending on the pre-treatment platelet counts.


Although Rituximab is considered to be a more intense immunosuppressive regimen compared to steroids, with no objective difference in timing of platelets response and the potential harmful outcome to induce virus replication, we did not use corticosteroids as the indicated first line treatment. Despite the high initial therapeutic efficacy, steroids achieve durable response in only 20-30%, often requiring ongoing or repeated administrations to maintain platelet counts, compared up to 50-70% therapeutic activity of Rituximab6,8. Our patient was debilitated from his previous treatment and could not tolerate a further long course of additional modalities. We also took into account that B-lymphocyte recovery occurs in 6–8 months after Rituximab infusion15 and liver-related effects of rituximab-containing regimens on HCV-positive CD20-positive B-cell Lymphoma patients, in most cases are not followed by major clinical events14,15.

In conclusion, this report underlines the significant response to anti-CD20 monoclonal antibody Rituximab, of a patient with severe PEG-INF related immune thrombocytopenia. In this context, physicians could be aware of anti-CD20 therapy as an alternative and efficacious option. From newer concepts, anti-CD20 treatment works by normalizing faulty T-cell responses, maintaining autoreactive T-cell activation and actually by restoring the defective tolerance-inducing to self antigens regulatory T cells that are essential in preventing autoimmunity14,17.

Conflict of interest
Authors report no conflict of interest.


